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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,018	10/12/2000	Philip Gotwals	A018	6239

7590 12/30/2004

Biogen Inc
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Cambridge, MA 02142

EXAMINER	
ANDRES, JANET L	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 12/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/423,018	GOTWALS ET AL.	
	Examiner	Art Unit	
	Janet L. Andres	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5 and 22-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *5* is/are allowed.

6)☒ Claim(s) *22-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 15 October 2004 has been entered.

Claims 5 and 22-29 are pending and under examination in this office action. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Objections Withdrawn

2. The objection to the specification is withdrawn in response to Applicant's amendment.

3. The rejections of claims 22-25 and 27-29 under 35 U.S.C. 112, first paragraph, as lacking enablement commensurate with the scope of the claims and as lacking written description is withdrawn in response to Applicant's amendment removing the term "equivalents".

Claim Rejections Maintained/New Grounds of Rejection

4. The rejection of claims 22-26 and 28 under 35 U.S.C. 103(a) as unpatentable over *Lin* in view of *Jacobs* is maintained for reasons of record in the office action of 20 April 2004 and newly applied to claim 27.

This rejection is newly applied to claim 27 because it appears to the Examiner that the extracellular domain of the *Lin* protein is >90% homologous to the extracellular domain of SEQ ID NO: 8 and fusions of the *Lin* protein are thus within the scope of claim 27.

Applicant's statement as to the availability of a recombinant human TGF-β sRII/Fc fusion protein beginning in July 1997 is acknowledged.

Applicant argues that impermissible hindsight has been used to combine the references, since the prior art must suggest the desirability of the invention. Applicant provides a declaration of Dr. Cate attesting to the difficulties encountered with the generation of analogous fusion proteins, citing the difficulties encountered by Dr. Cate in fusing the a constant region of an immunoglobulin with AMH-RII.

Applicant's arguments have been fully considered but have not been found to be persuasive. As was stated in the previous office actions, the *Lin* patent teaches a soluble type II receptor that binds TGF-β and teaches methods of using this receptor. *Jacobs* teaches that fusion of a soluble receptor with IgG results in improved function of the soluble receptor due to the resulting bivalency. It would be obvious to the artisan of ordinary skill, relying solely on the teachings of *Lin* and *Jacobs*, to modify the soluble protein taught by *Lin* using the methods of *Jacobs* in order to produce an IgG-TGF-β RII fusion protein. One of ordinary skill would have been motivated to do so because *Jacobs* teaches the advantages of such a fusion. It is not necessary that *Lin* specifically state that it would be desirable to produce such a fusion protein; the courts have held that:

Only a reason, suggestion or motivation need appear in the cited prior art in order to combine references under 35 U.S.C. 103. *Pro Mold Tool Col. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

and

Specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involves not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See CTS Corp. v. Electro Materials Corp. of America 202 USPQ 22 (DC SNY 1979); and In re Burckel 201 USPQ 67 (CCPA 1979).

and

In considering the disclosure of a reference, it is proper to take into account not only specific teaching of the reference but also the inferences which one skilled in the art would be reasonably be expected to draw therefrom In re Preda, 401 F.2d 825, 159 USPQ 342, 344 (CCPA 1968).

and

It is not necessary that the claimed invention be expressly suggested in any one or all of the references to justify combining their teachings; rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art *In re Keller,* 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

The declaration of Dr. Cate states that he was unable to produce a fusion protein using another type II receptor, the MIS receptor, and thus it was not predictable that the claimed invention could be made. Dr. Cate's declaration has been fully considered but has not been found to be persuasive. While Dr. Cate may have experienced difficulty in expression the MIS receptor fusion, the soluble region of the TGF-β R II has been fused with success to other proteins such as ubiquitin and glutathione-S-transferase. See U.S. patent 5,459,051, figure 7, and U.S. patent 5,545,569, column 27, lines 29-39. IgG fusion proteins had, at the time of Applicant's invention, been successfully generated with CD4, selectins and other adhesion molecules, several members of the TNF receptor family, other cytokine receptors including interferon γ receptor chains and interleukin receptors, and growth factor receptors. See Chamow et al. (Trends in Biotechnology, 1996, vol. 14, pp. 52-60), table 1 on pp. 54-55. Chamow et al. also teaches that "it is generally straightforward to construct immunoadhesins, to express them in mammalian cells, and to purify them" (p. 56, column 2). Thus Dr. Cate's single failure with a related protein does not serve to render success with the instantly claimed fusion proteins

unobvious, since soluble TGF-β type II receptors have been fused with other proteins, and fusion with immunoglobulins was well known and considered straightforward at the time of the invention.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 22-25 and 27-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims require that the claimed sequences correspond to all or part of the extracellular region of native TGF-β RII. It is appears that what is intended is that the sequences be at least 90% homologous to amino acids 1-160 of SEQ ID NO: 8 or 9 and they have been examined using this interpretation. However, there is no definition in the specification as to what relationship is intended by "corresponds". In addition, "native" TGF-β RII molecules have particular sequences which are not predictable; the artisan cannot know what sequences will occur in nature and thus be "native" unless a particular sequences has in fact been identified as occurring in an animal. Thus the artisan would not be able to determine what sequences Applicant intended the claims to encompass.

CLAIM 5 IS ALLOWED. CLAIMS 22-29 ARE REJECTED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Andres whose telephone number is 571-272-0867. The examiner can normally be reached on Monday, Tuesday, Thursday, Friday, 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Andres, Ph.D.
27 December 2004